ARADIGM

December 3, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Ref: Docket No. 02D-0254

Comments on Draft Guidance for Industry on:
Inhalation Drug Products Packaged in Semipermeable Container Closure Systems

Dear Sir or Madam:

Aradigm Corporation (Aradigm) appreciates the opportunity to provide the following comments on the **Draft Guidance for Industry, Inhalation Drug Products Packaged in Semipermeable Container Closure Systems.**

Aradigm recognizes that this guidance highlights a clinical concern primarily with inhalation product for the treatment of asthma and COPD. However, the CMC considerations in the draft guidance related to the specific issue of packaging in semipermeable container/closure system do not provide additional clarity to the information in the current guidances referenced in Section IV and are therefore redundant. Aradigm recommends that requirements specific to inhalation drug products packaged in semi-permeable material be clearly defined and that a clear distinction be made between chemical contaminants from packaging versus contaminants from the local environment. We also recommend that for completeness, the available guidances be modified rather than the issuance of an additional guidance.

Background

Lines 47-48 and 79-80: This guidance appears to be specific to patients with pulmonary disease (i.e., asthma and/or COPD) and to unit-dose vials. Clarity is requested on the applicability of this guidance to products not developed to treat pulmonary disease packaged in semi-permeable containers other than vials.

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Lines 55-60: We agree that careful choice of primary packaging can and should address the risk of contaminants from the primary packaging. The purpose of extractable and leachable testing is to address this specific issue. Clarity is requested to the reference to secondary and environmental contaminants. Which specific chemical, secondary and environmental contaminants are of concern or have been identified?

Section III CMC Considerations

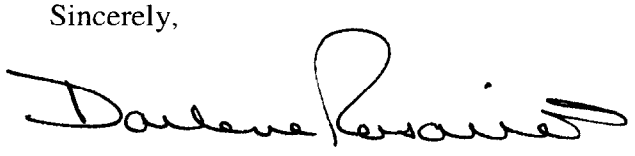
Line 77-93: This paragraph implies that the products developed to treat pulmonary disease, which may be contaminated by chemicals from the environment, may be a reason for the increase in the asthma mortality rate. However, patients are continually exposed to these same contaminants in the environment and most likely at increased levels. In addition, no data exist that attribute adverse reactions to chemical contaminants from the product type identified in this guidance, yet the Agency is imposing this additional requirement on the manufacturers of these types of products which will increase the cost of drug development and therefore impact cost to the patient.

Line 96-99: Clarity is requested on the applicability of this guidance specifically to unit-dose vials where shelf-life storage is in LDPE primary packaging and secondary carton.

This guidance needs to evaluate other considerations such as shelf-life storage conditions and in-use periods, which minimize the exposure of product to the local environment. The requirement for secondary packaging should be product specific and take into consideration therapeutic indication.

Aradigm appreciates the opportunity to provide comments to this guidance. Please feel free to contact me to discuss or seek clarification to our comments.

Sincerely,



Darlene Rosario
Director, Regulatory Affairs